15. (4x amended) A method for treating a subject having a defect in long-term memory, which comprises administering to the subject a compound that inhibits binding of (i) a cAMP-responsive-element-binding-protein-2 having an amino acid sequence identical to the sequence set forth in SEQ ID NO:1 to (ii) a transcription factor protein and/or DNA, wherein the protein or DNA is an activator of cAMP-responsive gene expression, and wherein the compound is administered in an amount effective to treat said memory defect in the subject.

REMARKS

Claims 1, 3-6, 15, 16 and 18-22 are pending. Claims 1, 3-6 and 21 have been canceled. Claim 15 has been amended to more specifically set forth what applicants regard as the invention. Support for these amendments may be found in the specification, *inter alia*, on page 22, line 33, through page 23, line 2 and on page 34, line 30 through page 35, line 28. Applicants submit that these amendments raise no issue of new matter. Thus, claims 15, 16, 18-20 and 22 are now pending and under examination.

Pursuant to the requirements of 37 C.F.R. 1.121, applicants annex hereto as Exhibit A a copy of the amended claims marked up to show the changes made herein relative to the previous version thereof.

In view of the arguments set forth below, applicants maintain that the Examiner's rejections made in the June 19, 2001 Office Action have been overcome, and respectfully request that the Examiner reconsider and withdraw same.

Withdrawal Under 37 C.F.R. 1.142(b)

The Examiner withdrew claims 1 and 3-6 from consideration as allegedly directed to a non-elected invention. Without conceding the correctness of the Examiner's claim withdrawal, applicants point out that claims 1 and 3-6 have been canceled, rendering the withdrawal moot.

Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 15, 16 and 18-22 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to allow one skilled in the relevant art to which it pertains to make and/or use the invention commensurate in scope with the claims.

In response to the rejection of claim 21, applicants point out that this claim has been canceled. Thus, the rejection thereof is now moot.

In response to the rejection of claims 15, 16, 18-20 and 22, applicants respectfully traverse.

Briefly, claim 15 provides a method for treating a subject having a defect in long-term memory. This treatment comprises administering a compound that inhibits the binding of SEQ ID NO:1 to either a transcription factor protein or a DNA, or both, wherein the protein or DNA is an activator of cAMP-dependent gene expression. Dependent claims 16, 18-20 and 22 provide various embodiments of the method of claim 15.

The Examiner's rejection is based upon two assertions. The first assertion is that enablement does not exist for a "human homologue" as recited in claim 15 with respect to the *Aplysia* protein having SEQ ID NO:1. Without conceding the correctness of the Examiner's position, applicants point out that claim 15, as amended, does not recite the phrase "human homologue".

The Examiner's second assertion is that the claimed method is not enabled for improving long-term memory in all subjects, even though the method is enabled in subjects such as *Aplysia* and *Drosophila*.

Applicants respectfully disagree, and maintain that one of skill would reasonably expect the method of claim 15 to succeed in vertebrate subjects. This position is based on a connection between long-term memory formation in *Aplysia* and long-term memory formation in vertebrate subjects, as clearly taught by the specification and the art.

Specifically, the protein CREB1 is required for long-term memory in both *Aplysia* and mammals. Bourtchuladze *et al* (1994), already of record, demonstrate this finding. That is, this reference teaches a connection between (i) long-term facilitation (the cellular model of long-term memory in *Aplysia*), (ii) long-term memory in mice (as measured in behavioral assays), and (iii) long-term potentiation in the mammalian hippocampus (the cellular model of long-term memory in mammals). The protein CREB1 is required for long-term memory in each of these three systems. That a requirement for CREB1 for long-term memory exists in both invertebrates and vertebrates is also made clear in the specification at page 22, line 33 through page 23, line 2.

CREB2 (SEQ ID NO:1) is a potent inhibitor of CREB1, as demonstrated in Example 2 of the specification, and this ability of CREB2 to repress CREB1 is conserved among humans, *Drosophila*, and *Aplysia* (Karpinski (1992), and Yin (1994), both of record).

Moreover, compounds that inhibit the binding of CREB2 (SEQ ID NO:1) to either DNA or other proteins increase synaptic connections, as shown in the specification on page 34, line 30 through page 35, line 28. This increase in synaptic connections is "the most reliable anatomical measure of long-term memory" in both vertebrate and invertebrate subjects (page 411 of Bailey and Kandel, of record). So, according to this measure, such inhibitory compounds would reasonably be expected to increase long-term memory in both vertebrate and invertebrate subjects.

For these reasons, applicants maintain that, at the time of filing, one of skill in the art would have expected the instant invention to succeed in both vertebrate and invertebrate subjects.

Thus, applicants maintain that claim 15 is enabled. Likewise, applicants maintain that dependent claims 16, 18-20 and 22 are also enabled.

The Examiner also rejected claims 15, 16 and 18-22 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

In response to the rejection of claim 21, applicants point out that this claim has been canceled. Thus, the rejection thereof is now moot.

In response to the rejection of claims 15, 16, 18-20 and 22, applicants respectfully traverse.

Claims 15, 16, 18-20 and 22 are described above.

As with the enablement rejection above, this rejection is also based on the recitation of the phrase "human homologue" in claim 15 with respect to the *Aplysia* protein having SEQ ID NO:1.

Without conceding the correctness of the Examiner's position, applicants again point out that claim 15 does not recite such phrase and that, accordingly, claims 15, 16, 18-20 and 22 satisfy the written description requirement.

In view of the above remarks, applicants maintain that claims 15, 16, 18-20 and 22 satisfy the requirements of U.S.C. §112, first paragraph.

Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 15, 16 and 18-22 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

In response to the rejection of claim 21, applicants point out that this claim has been canceled. Thus, the rejection thereof is now moot.

In response to the rejection of claims 15, 16, 18-20 and 22, applicants respectfully traverse.

Claims 15, 16, 18-20 and 22 are described above.

This rejection is based upon the recitation of the phrase "human homologue" in claim 15. Allegedly, the metes and bounds of this term are not clear, thereby rendering the claims indefinite.

Applicants note, without conceding the correctness of the Examiner's position, that claim 15, as amended, does not recite the term "human homologue." Applicants maintain that the language of claim 15 is both clear and definite.

In view of the above remarks, applicants maintain that claims 15, 16, 18-20 and 22 satisfy the requirements of U.S.C. §112, second paragraph.

Rejection Under 35 U.S.C. §102(b)

The Examiner rejected claims 15, 16 and 18-22 under 35 U.S.C. §102(b) as allegedly anticipated by Dash *et al* (1990).

In response to the rejection of claim 21, applicants point out that this claim has been canceled. Thus, the rejection thereof is now moot.

In response to the rejection of claims 15, 16, 18-20 and 22, applicants respectfully traverse.

Claims 15, 16, 18-20, and 22 are described above.

In relevant part, claim 15 provides a method of *treating* a subject having a *defect* in long-term memory.

Briefly, Dash *et al* teach that the injection of an oligonucleotide comprising a cAMP-responsive element (CRE) into the nucleus of *Aplysia* sensory neurons blocks long-term facilitation.

In order to anticipate a claim, a reference must teach every element of the claim, either expressly or inherently. The Dash reference fails to teach all elements of claim 15 since it does not teach a method for treating a subject with a defect in long-term memory. Thus, Dash *et al* do not anticipate the method of claim 15, nor those of dependent claims 16, 18-20 and 22.

In view of the above remarks, applicants maintain that claims 15, 16, 18-20 and 22 satisfy the requirements of 35 U.S.C. §102(b).

Summary

In view of the amendments and remarks made herein, applicants maintain that the claims pending in this application are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the enclosed $460.00 extension fee, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

Assistant Commissioner for Patents, Washington, D.C. 20231

12/18/01

Alan J. Morrison
Reg. No. 37,399

Date

Marked-up Version of the Amended Claims

15. (4x amended) A method for treating a subject [an animal] having [with] a defect in long-term memory [defect due to binding of a cAMP-responsive-element-binding-protein-2 to a transcription factor protein or to DNA associated with cAMP-responsive gene expression] which comprises administering to the subject [animal] a compound that inhibits binding of (i) a [the] cAMP-responsive-element-binding-protein-2 having an amino acid sequence identical to the sequence set forth in SEQ ID NO:1 [or a human homologue thereof], to (ii) a [the] transcription factor protein and/or [to the] DNA wherein the protein or DNA is an activator of cAMP-responsive gene expression, and wherein the compound is administered in an amount effective to [inhibit binding and thereby] treat said memory defect in the subject [animal].